

MSH3 Biallelic gene

Associated Syndrome Name: MSH3-associated polyposis syndrome

MSH3 Biallelic Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Colorectal	Elevated Risk

MSH3 Biallelic gene Overview

MSH3-associated polyposis syndrome ^{1, 2}

- Individuals with mutations in both copies of the *MSH3* gene (biallelic mutations) have *MSH3*-associated polyposis syndrome. *MSH3*-associated polyposis syndrome has been found in a small number of individuals with greater than 20 colorectal polyps and a history of colorectal and other cancers. The polyps are mostly adenomas, which is expected to lead to an increased risk for colorectal cancer. Although there are as yet no precise estimates of the colorectal cancer risk associated with *MSH3*-associated polyposis syndrome, it is possible that this risk is significantly increased over that in the general population.
- The small number of individuals identified to date with *MSH3*-associated polyposis syndrome have been diagnosed with a wide variety of other types of cancer and precancerous adenomas involving the brain, stomach, thyroid and small intestine. However, more studies are needed to determine the types of cancer associated with *MSH3*-associated polyposis syndrome and the exact size of the risks. At this time there are no professional society guidelines for the management of these risks.
- Although there is an increased risk for colorectal cancer in individuals with *MSH3*-associated polyposis syndrome, it may be possible to reduce this risk with appropriate medical management. Guidelines for the medical management of individuals with *MSH3*-associated polyposis syndrome have been developed by the National Comprehensive Cancer Network (NCCN). These are listed below. These guidelines will evolve as we learn more, and it is recommended that patients with *MSH3*-associated polyposis syndrome be managed by a multidisciplinary team with expertise in medical genetics and the care of patients with hereditary cancer syndromes.

MSH3 Biallelic gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Colorectal	To age 80 ^{1, 3, 4}	Elevated risk	2.8%

MSH3 Biallelic Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Colorectal	Colonoscopy ²	25 to 30 years	Every 2 to 3 years
	Colorectal surgical evaluation and counseling. ²	Based on cancer diagnosis and/or polyp number, size and histology	NA

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the *MSH3* Biallelic gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

Since this patient has mutations in both copies of the *MSH3* gene, it is almost certain each of their parents and all of their children carry at least one of these *MSH3* mutations. Siblings are at very high risk for carrying either one or two *MSH3* mutations. The cancer risk table that follows provides cancer risks for individuals with mutations in both copies (biallelic) of the *MSH3* gene. These risks do not apply to relatives who have inherited only a single *MSH3* mutation (monoallelic).

References

1. Adam R, et al. Exome Sequencing Identifies Biallelic *MSH3* Germline Mutations as a Recessive Subtype of Colorectal Adenomatous Polyposis. *Am J Hum Genet.* 2016 99:337-51. PMID: 27476653.
2. Gupta S, et al. NCCN Clinical Practice Guidelines in Oncology[®] Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric. V 4.2024. Apr 2. Available at <https://www.nccn.org>.
3. Aelvoet AS, et al. A large family with *MSH3*-related polyposis. *Fam Cancer.* 2022. Epub ahead of print. PMID: 35675019.
4. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2025 Apr 1]. Available from <https://seer.cancer.gov/explorer/>.

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